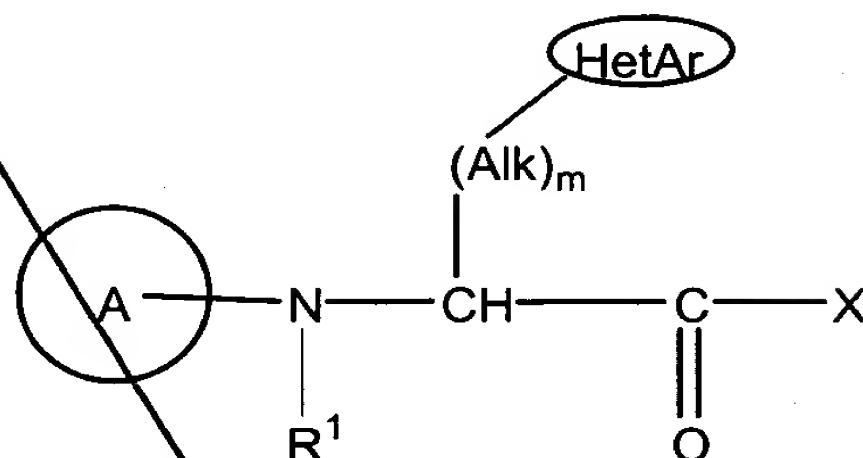


WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I)

wherein:

A is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)₂-alkyl, -OS(O)₂-substituted alkyl, -OS(O)₂-aryl, -OS(O)₂-substituted aryl, -OS(O)₂-heteroaryl,

contd.
a¹⁸

5 -OS(O)₂-substituted heteroaryl, -OS(O)₂-heterocyclic, -OS(O)₂-substituted heterocyclic, -OSO₂-NRR where each R is independently hydrogen or alkyl, -NRS(O)₂-alkyl, -NRS(O)₂-substituted alkyl, -NRS(O)₂-aryl, -NRS(O)₂-substituted aryl, -NRS(O)₂-heteroaryl, -NRS(O)₂-substituted heteroaryl, -NRS(O)₂-heterocyclic, -NRS(O)₂-substituted heterocyclic, -NRS(O)₂-NR-alkyl, -NRS(O)₂-NR-substituted alkyl, -NRS(O)₂-NR-aryl, -NRS(O)₂-NR-substituted aryl, -NRS(O)₂-NR-heteroaryl, -NRS(O)₂-NR-substituted heteroaryl, -NRS(O)₂-NR-heterocyclic, -NRS(O)₂-NR-substituted heterocyclic where R is hydrogen or alkyl, -N[S(O)₂-R']₂ and -N[S(O)₂-NR']₂ where
10 each R' is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HetAr is a nitrogen containing heteroaryl or a nitrogen containing substituted heteroaryl group;

15 Alk is an alkylene group of 1 to 4 carbons;

m is 0 or 1;

R¹ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl,
20 heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxo, substituted cycloalkenoxo, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR''R'' where each R'' is independently
25 selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

contd.
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and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula (I) has a binding affinity to VLA-4 as expressed by an IC_{50} of about $15\mu M$ or less.

5

2. The compound of Claim 1 wherein HetAr is a nitrogen containing substituted heteroaryl group.

3. The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group that is substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino oxysulfonyl, aryl and substituted aryl.

4. The compound of Claim 1 wherein HetAr is a nitrogen containing heteroaryl group is substituted with a group of formula $-O-Z-NR^{11}R^{11'}$ or $-O-Z-R^{12}$ wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of $-C(O)-$ and $-SO_2-$.

5. The compound of Claim 4 wherein the nitrogen containing heteroaryl group is substituted with a group of formula $-OC(O)NR^{11}R^{11'}$ wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of

6. The compound of Claim 5 wherein the nitrogen containing heteroaryl group is substituted with $-\text{OC}(\text{O})\text{N}(\text{CH}_3)_2$.

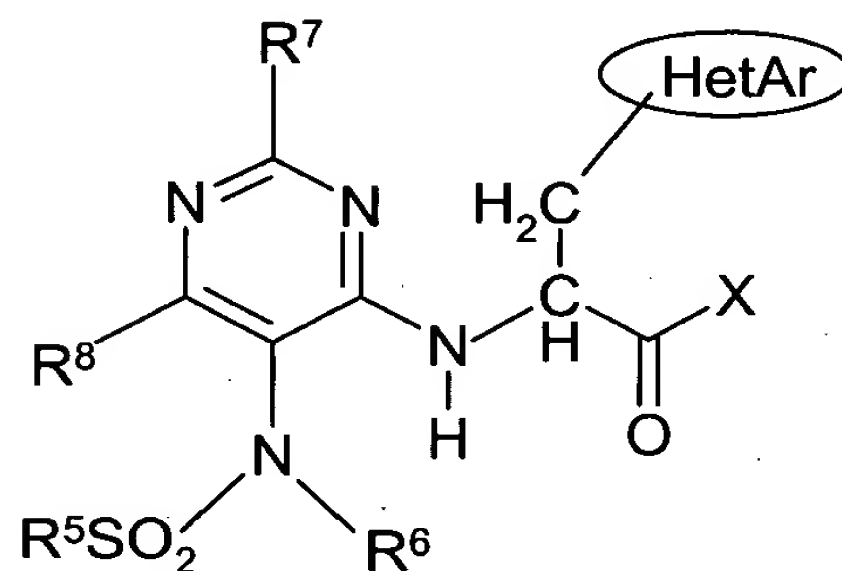
Amen.
a¹

RECORD OF THE PROCEEDINGS

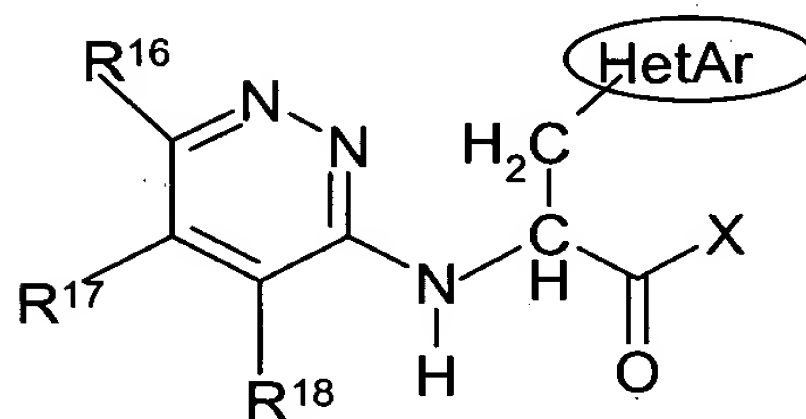
9. The compound of Claim 8 wherein A is 1-oxo-1,2,5-thiadiazole, 1,1-dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine ring which is optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

10. The compound of Claims 1 to 9 wherein R¹ is hydrogen, and X is hydroxyl.

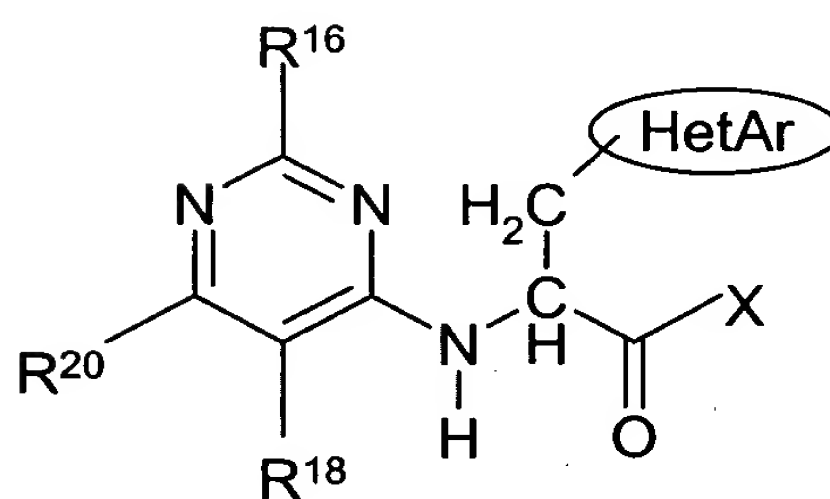
11. The compound of Claim 1 wherein the compound has formula IIa, IIb, IIc, IId, or IId:



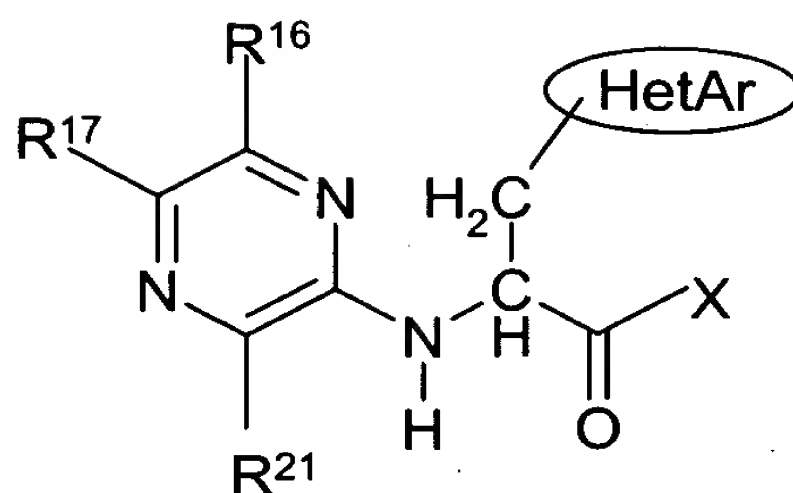
IIa



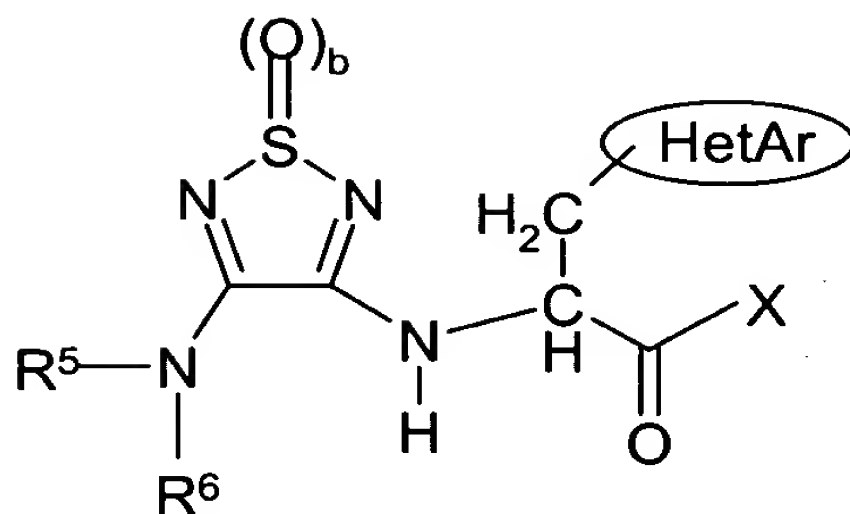
IIb



IIc



IIId,



IIe

5

wherein:

HetAr is a nitrogen containing heteroaryl group substituted with a
 substituent selected from the group consisting of acyl, acylamino, acyloxy,
 10 aminoacyl, aminocarbonylamino, aminothiocarbonylamino,
 aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino,
 thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl,
 oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R⁵ is selected from the group consisting of alkyl, substituted alkyl,
 15 alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted

cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R^6 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and $-SO_2R^{10}$ where R^{10} is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

X is hydroxyl; and
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

5 12. The compound of Claim 11 wherein the compound is selected from formula IIc, IId or IIe.

10 13. The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula -O-Z-NR¹¹R^{11'} or -O-Z-R¹² wherein R¹¹ and R^{11'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-.

15 14. The compound of Claim 13 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -OC(O)NR¹¹R^{11'} wherein R¹¹ and R^{11'} are independently selected from the group consisting of alkyl or R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle.

20 15. The compound of Claim 14 wherein the nitrogen containing heteroaryl group is substituted with -OC(O)N(CH₃)₂ and is at the para position of the heteroaryl group.

25 16. The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with an aryl or substituted aryl group.

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Amend.
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17. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1 to 16.

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18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1-16.

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